Integrated chemical genomics reveals modifiers of survival in human embryonic stem cells.

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Authors: Robert Damoiseaux, Sean P Sherman, Jackelyn A Alva, Cory Peterson, April D Pyle

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Public Summary:

Scientific Abstract:
Understanding how survival is regulated in human embryonic stem cells (hESCs) could improve expansion of stem cells for production of cells for regenerative therapy. There is great variability in comparing the differentiation potential of multiple hESC lines. One reason for this is poor survival upon dissociation, which limits selection of homogeneous populations of cells. Understanding the complexity of survival signals has been hindered by the lack of a reproducible system to identify modulators of survival in pluripotent cells. We therefore developed a high-content screening approach with small molecules to examine hESC survival. We have identified novel small molecules that improve survival by inhibiting either Rho-kinase or protein kinase C. Importantly, small molecule targets were verified using short hairpin RNA. Rescreening with stable hESCs that were genetically altered to have increased survival enabled us to identify groups of pathway targets that are important for modifying survival. Understanding how survival is regulated in hESCs could overcome severe technical difficulties in the field, namely expansion of stem cells to improve production of cells and tissues for regenerative therapy.